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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/604,693	06/27/2000	Markus Pompejus	BGI-130CP	4996

959 7590 10/19/2005

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/604,693	POMPEJUS ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6,10-16 and 39-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,4,39,40* is/are allowed.

6)☒ Claim(s) *6,10-16 and 41-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants addition of new claims 45 and 46, in the paper 7/28/2005, is acknowledged. Claims 1, 4, 6, 10-16 and 39-46 are at issue and are present for examination.

Applicants' arguments filed on 7/28/2005, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Information Disclosure Statement

Applicants filing of the information disclosure statement filed on 7/28/2005 is acknowledged. Those references, D1 and D2 have not been initialed.

Specification

The disclosure is objected to because of the following informalities:

It was previously pointed out to applicants and objected to, that on page 28, lines 11-14, of the specification applicants state "As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% homologous to each other typically remain hybridized to each other..." Such a statement that nucleotide sequences which are 60% homologous would hybridize under stringent conditions is considered to be repugnant to what is known in the art.

Applicants traverse this objection on the grounds that the above is not repugnant to what is known in the art as evidenced by, for example U.S. Patent No. 6,436,684 which makes similar statements.

Applicants complete argument is acknowledged, however, found nonpersuasive on the basis that the reliance of applicants on another patent application is not considered an accurate reflection of what is considered to be "known in the art". The objection however is withdrawn because it is recognized that sequences at least 60% homologous to each other do typically remain hybridized to each other when hybridization conditions are under stringent conditions, and when those sequences are at least 90% or 95% homologous to each other. As sequences which are at least 90% or 95% homologous to each other, are at least 60% homologous to each other, the objection is withdrawn.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 10-16 and 41-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2,

and vectors and host cells comprising said nucleic acid, does not reasonably provide enablement for any isolated nucleic acid molecule comprises a nucleotide sequence which is a mere 90% identical to the nucleotide sequence of SEQ ID NO: 1, wherein said nucleic acid molecule encodes a polypeptide which is capable of functioning as an extracellular nuclease, and vectors and host cells comprising said nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In response to this previous rejection applicants have added new claims 45 and 46 and traverse the rejection as it applies to the rejected claims. Claims 45 ad 46 are included in the rejection for the reasons previously stated for claims 6, 10-16 and 41-44.

Applicants traverse the rejection based on the following reasons: Applicants first submit that Example 14 of the *Revised Interim Written Description Guidelines Training Materials* provides that a claim directed to variants of a protein having SEQ ID NO: 3 and catalyze the reaction of A-B with an accompanying specification that discloses a single species falling within the claimed genus satisfies the requirements of 35 U.S.C. 112 first paragraph for written description. Applicants further submit that the rationale for this position is that the single species disclosed is representative of the genus because all of the members have at least 95% structural identity and because of the presence of an assay which applicants provided for identifying all of the 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity.

Applicants further submit that the Guidelines also provide that the procedures for making variants are conventional in the art.

Applicants submit that in the present case claims 6 and 41 are directed to nucleic acid molecules that are at least 90% or 95% identical to SEQ ID NO: 1 wherein the molecule encodes a polypeptide having extracellular nuclease activity. Applicants further submit that applicants have disclosed assays for identifying all of the at least 90% or 95% identical nucleic acids that encode a polypeptide having extracellular nuclease activity. Applicants thus submit that based on the foregoing teachings in applicants specification, as well as the general knowledge in the art at the time of filing of the claimed invention, one of skill in the art would be able to make and use the claimed invention using only routine experimentation.

Applicants complete argument is acknowledged, however, found non-persuasive for the following. First applicants are reminded that the current rejection is based on a lack of enablement, not a lack of written description. Second while examples in the *Revised Interim Written Description Guidelines Training Materials* are helpful for using to determine if a claimed genus is adequately described, they are only guidelines, and in addition to any guidelines for written description or enablement, a number of other application specific variables must be considered in order to determine whether a claimed genus is both adequately described and sufficiently enabled (i.e. the Wands factors etc...). Since the instant rejection is under 112 first paragraph for a lack of enablement, those factors which are considered in determining if the claimed genus meet the requirements of the statue are the Wands factors. In considering the Wands

factors, it is noted that applicants have argued that the state of the art and skill of those in the art is high, such that methods of making variants of a known nucleic acid sequence are conventional. While this may be true, it remains that the art as well as applicants specification provide no substantial amount of direction or guidance as to the direction one of skill in the art must take to make and use those variants of the claimed genus.

While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., encoding a extracellular nuclease) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting "extracellular nuclease" activity; (B) the general tolerance of "extracellular nuclease" to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of an "extracellular nuclease" with an expectation of obtaining the desired

biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the "extracellular nuclease" activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those nucleic acid molecules of the claimed genus encoding polypeptides with the claimed "extracellular nuclease" activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any isolated nucleic acid molecule comprises a nucleotide sequence at least 90% or 95% identical to the nucleotide sequence of SEQ ID NO: 1, wherein said nucleic acid molecule encodes a polypeptide which is capable of functioning as an extracellular nuclease. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
10/4/2005